

## Myasthenia gravis associated with autoimmune diseases of the thyroid gland –a series of cases.

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### Abstract

**Background:** We analysed retrospectively the therapeutic results of thymic pathology associated with thyroid disease, in relation to demographic data, clinical severity of the diseases and pathological nature of the diseases.

**Method:** This is a retrospective case-series of thymopathies associated with thyroid pathology, treated in a single academic institution, third surgery unit, "St. Spiridon Hospital", Iași, from 1985 till 2015. Out of 99 cases of diagnosed and treated thymus pathology, we recorded 8 cases of thymopathies associated with thyroid disease. This association is a rare one and challenging as management strategies.

**Results:** In all cases thymic pathology was diagnosed during thyroid disease. In this series there is a female predominance. Four patients had below 50 years of age and included in the early-onset Myasthenia Gravis.

**Conclusions:** Autoimmune thyroid disease may be associated with thymic hyperplasia, in which no surgical action should be taken, regarding the thymus with thymoma surgical treatment is essential. When Graves' and thymoma are associated, total thyroidectomy is advisable instead of medical treatment, in which is included beta blockers contraindicated in myasthenia gravis. Total thyroidectomy and thymectomy can be performed at the same stage if the clinical condition of the patient is fit for both operations or in stages.

**Key words:** Myasthenia gravis, thyroid autoimmunity, thymoma

### Introduction

Autoimmune disease includes the pathologies that are defined by the specific immune responses directed against the structures of the self-components.

Myasthenia gravis (MG) is a chronic autoimmune disorder that affects the neuromuscular junction of the skeletal muscles, blocking the synaptic neurotransmission, causing weakness and an abnormal fatigability [1]. The mechanism involved in this disease includes the production of antibodies against the acetylcholine receptor (AChR), tyrosine kinase and a grin receptor low-density lipoprotein receptor-related protein-4 antibody (LRP4) [2].

Autoimmune thyroid disease is a group of pathologies that includes the Graves' Disease (GD) - hyperthyroidism, Hashimoto's thyroiditis (HT) - hypothyroidism and euthyroid patients with positive anti-

thyroid autoantibodies. [3] GD is caused by thyrotoxicosis that develops when the body produces antibodies against the thyroid-stimulating hormone receptor (TSH-R), that evolves with ophthalmopathy, dermopathy, acropathy. [4]

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The pathologic features of HT include gradual atrophy and fibrosis of the thyroid gland due to lymphocytic infiltration and follicular destruction. It is the most frequent autoimmune thyroid disorder that causes hypothyroidism in demographic regions with iodine enough apport. [5] Anti-TSH antibodies blocks the TSH receptor in HT but stimulate the TSH receptor in GD.

The thymoma is a neoplasia derived from the thymus gland, from epithelial cells, consider to be the most common mediastinal masses, with the develop in the anterior mediastinum in about 50% of reported cases. [6]

Thymus and thyroid gland are both implicated in the normal development of the body, the thymus being responsible for the progress of the cellular immunity while thyroid hormones regulate the cellular metabolism. [7]

When thymus pathology interferes thyropathies, therapeutic strategies should be individualized after an accurate diagnostic work up. Each disease may aggravate the other, the weakness of the muscles is present in both conditions and may be attributed to other diseases such as neurasthenia, hypocalcaemia. Delaying the diagnoses is an unfavourable prognosis factor.

What is the role of surgery in these cases? It depends on the severity of the diseases and underlying pathology. Other factors such as age, the history of each disease, the response to medical treatment, comorbidities may contribute to the outcome.

The aim of this study was to analyse retrospectively the therapeutic results of thymic pathology associated with thyroid disease, in relation to demographic data, clinical severity of the diseases and pathological nature of the diseases.

## Material and methods

This is a retrospective case-series of thymopathies associated with thyroid pathology, treated in

a single academic institution, third surgery unit, “St. Spiridon Hospital”, Iasi, from 1985 till 2019. Out of 99 cases of diagnosed and treated thymus pathology, we recorded 8 cases of thymopathies associated with thyroid disease. This association is a rare one and challenging as management strategies.

The clinical severity of MG was assessed after MGFA (MG Foundation of America) classification:

- Class I: Any ocular muscle weakness;
- Class II: Mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity;
  - Class IIa: Predominantly affecting limb, axial muscles, or both;
  - Class IIb: Predominantly affecting oropharyngeal, respiratory muscles, or both;
- Class III: Moderate weakness affecting other than ocular muscle; may also have ocular muscle weakness of any severity;
  - Class IIIa: Predominantly affecting limb, axial muscles, or both;
  - Class IIIb MG: Predominantly affecting oropharyngeal, respiratory muscles, or both;
- Class IV: Severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity;
  - Class IVa: Predominantly affecting limb, axial muscles, or both;
  - Class IVb: Predominantly affecting oropharyngeal, respiratory muscles, or both;
- Class V: Defined by intubation. [8]

Thymomas were classified after 2015 World Health Organisation (WHO) classification:

| Thymoma subtype         | Obligatory Criteria                                                                                                                                                                                                                       | Optional Criteria                                            |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| Type A                  | Occurrence of bland, spindle-shaped epithelial cells (at least focally); paucity <sup>a</sup> or absence of immature (TdT+) T cells throughout the tumour                                                                                 | Polygonal epithelial cells; CD20+ epithelial cells           |
| Atypical type A variant | Criteria of type A thymoma; in addition, comedo-type tumour necrosis; increased mitotic count (>4/2mm <sup>2</sup> ); nuclear crowding                                                                                                    | Polygonal epithelial cells; CD20+ epithelial cells           |
| Type AB                 | Occurrence of bland, spindle-shaped epithelial cells (at least focally); abundance of immature (TdT+) T cells focally or throughout tumour                                                                                                | Polygonal epithelial cells; CD20+ epithelial cells           |
| Type B1                 | Thymus-like architecture and cytology: abundance of immature T cells, areas of medullary differentiation (medullary islands); paucity of polygonal or dendritic epithelia cells without clustering (i.e., <3 contiguous epithelial cells) | Hassall's corpuscles; perivascular spaces                    |
| Type B2                 | Increased numbers of single or clustered polygonal or dendritic epithelial cells intermingled with abundant immature T cells                                                                                                              | Medullary islands; Hassall's corpuscles; perivascular spaces |
| Type B3                 | Sheets of polygonal slightly to moderately                                                                                                                                                                                                | Hassall's corpuscles; perivascular                           |

|                     |                                                                                                                                         |                                                                                  |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
|                     | atypical epithelial cells; absent or rare intercellular bridges; paucity or absence of intermingled TdT <sup>+</sup> T cells            | spaces                                                                           |
| MNT <sup>b</sup>    | Nodules of bland spindle or oval epithelial cells surrounded by an epithelial cell-free lymphoid stroma                                 | Lymphoid follicles; monoclonal B cells and/or plasma cells (rare)                |
| Metaplastic thymoma | Biphasic tumour composed of solid areas of epithelial cells in a background of bland-looking spindle cells; absence of immature T cells | Pleomorphism of epithelial cells; actin, keratin, or EMA- positive spindle cells |

The atypical type A thymoma variant (in bold) is the only new addition to the “historic” list of thymoma subtypes.

<sup>a</sup>Paucity versus abundance: any area of crowded immature T cells or moderate numbers of immature T cells in more than 10% of the investigated tumour are indicative of “abundance.”

<sup>b</sup>Microscopic thymoma, sclerosing thymoma, lipofibroadenoma. [9]

### Clinical subtypes of MG in relation with detected antibodies. [10]

| Subtypes                    | Characteristics                                                                                                                                                   |
|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ocular MG                   | Purely ocular symptoms, no evidence of thymoma, anti-AChR antibody positive in 50%                                                                                |
| Early-onset MG              | Age of onset < 50 years, thymic hyperplasia, usually females, antibodies against AChR                                                                             |
| Late-onset                  | MG Age of onset > 50 years, normal or atrophic thymus, mainly males, presence of antibodies against AChR, titin, RyR                                              |
| Thymoma-associated MG       | Age of onset between 40 and 60 years, thymic neoplasia, antibodies against AChR, titin, RyR and voltage-gated K <sup>+</sup> channel subfamily A member 4 (KCNA4) |
| MuSK antibody-associated MG | Onset age < 40 years in most patients, normal thymus, antibodies against MuSK                                                                                     |
| Seronegative MG             | Variable muscular involvement and severity, variable age of onset, thymic hyperplasia in some patients, no detectable antibodies against AChR and MuSK, LRP4      |

MG: myasthenia gravis; MuSK: muscle-specific tyrosine kinase; AChR: acetylcholine receptors; RyR: ryanodine receptor, lipoprotein related protein receptor 4.

Apart from immunological serum tests (anti-AChR, anti-MuSK) MG was documented with short-acting anticholinesterase drug- positive test, electromyography - increased decrement>15% (EMG-D).

Chest CT scan as the gold standard imaging procedure in patients with MG was done in all patients, giving us information about the morphology of the thymus (size, density, limits).

In equivocal cases, we started to perform a functional investigation of the thymus by radionuclide scintigraphy with Tc 99. Corroborating all clinical and investigations data, a multidisciplinary team (neurologist, endocrinologist, surgeon, anaesthetist) agreed on adequate therapeutic decision, according to the clinical severity of disease, the patient's age, the degree of functional impairment and the high index of suspicion of thymoma. When thymic pathology is associated with thyropathies the therapeutic decision is directed to which comes first for surgery.

Thymectomy was indicated in this series when generalized MG was aggravating by not responding to medical treatment and in case of high suspicion or evidence of thymoma. GD associated with MG is best treated surgically to avoid beta-blockers that may aggravate myasthenia gravis.

#### Results

Out of 99 cases of thymopathies treated in our unit, 8 cases were associated thyroid disease

MG- GD-3 cases

MG- HT-3 cases

MG- HT-haemolytic anemia-1 case

MG (Thymoma) - Toxic multinodular goitre- 1 case

Table 1- characteristics of patients, surgical treatment and outcome

| Nr | Age | Sex | Diagnosis      | Ab.achr/<br>Ab.musk | Pathology   | Surgery | Outcome                                          |
|----|-----|-----|----------------|---------------------|-------------|---------|--------------------------------------------------|
| 1  | 33  | F   | GD/MGIVA       | +/-                 | MC on Grave | TT      | death-28poday CRF                                |
| 2  | 42  | F   | GD /MGIIIA     | +/-                 | Grave       | TT      | MG ameliorated                                   |
| 3  | 54  | F   | GD/MGIIA       | +/-                 | Grave/BTy   | TT/ET   | MG ameliorated                                   |
| 4  | 54  | F   | HT/MGIVB       | +/-                 | TLH         | ET      | Death 2 mpoMSOF                                  |
| 5  | 28  | F   | HT/ MGIIA      | +/-                 | TLH         | ET      | MG, complete remission                           |
| 6  | 64  | F   | HT/MGIVA       | +/-                 | ITy         | ET      | MG ameliorated/<br>death at 7 years po, CRF      |
| 7  | 19  | M   | H/TMGI/HA      | -/-                 | TLH         | ET      | Constrictive pericarditis;<br>complete remission |
| 8  | 46  | F   | TMNG/<br>MGIVA | +/-                 | MNG/ITy     | TT/ET   | ameliorated, death at 1 year,<br>CRF             |

MG with MGFA classification, HA-haemolytic anaemia, MC-microcarcinoma, BTy-benign thymoma, TLH-thymic lymphoid hyperplasia, TT-total thyroidectomy, ET-extended thymectomy, ITy-invasive thymoma, TMNG-toxic multinodular goitre, ETy-ectopic thymoma, CRF - cardio-respiratory failure.

In all cases thymic pathology was diagnosed during thyroid disease. In this series there is a female predominance. Four patients had below 50 years of age and included in the early onset MG with positive antibodies against AChR and negative for MuSK. Four patients who died in postoperative period had a severe clinical form of myasthenia gravis.

#### MGand Grave's disease

##### Case 1

JM, 33-year-old woman presented history of progressive and refractory MG for one month. According to MGFA clinical classification, on admission it was an IVa class.

She was known with GD for 10 years, untreated due to an anaphylactic shock to anti-thyroid drugs. Thyroid gland volume - 28.9 ml, TSH-0.2mU/l (n-0,4-7) Ft4-2.6 nmol/dl, CT scan showed a diffuse compressive goitre. (Fig.1)



Figure 1: CT scan of the neck-compressive goitre



Figure 2: CT scan of the thorax- enlarged thymus gland

Myasthenic profile: EMG-D-30%, positive antiChE test, CT scan suggestive for thymic lymphoid hyperplasia (Fig.2), Ab. AChR-24 nmol/dl (n-0,25). The treatment with anticholinesterase drugs and steroids was without effect. Considering MG secondary to hyperthyroidism, total thyroidectomy was performed after 10 days of Lugol solution administration. We expected the thymic lymphoid hyperplasia to regress along with myasthenic symptoms after surgery. Pathology report revealed bilateral micropapillary carcinoma on GD. The postoperative course was complicated with acute respiratory failure requiring mechanical ventilation. Rescue treatment of myasthenic crisis consisting in repeated plasmapheresis sessions, intravenous steroids was without results and the patient died in the 28<sup>th</sup> postoperative day by cardio-respiratory arrest.

## Case 2

A.I. 42-year-old woman was diagnosed with GD 5 years ago and in the last 6 months developed generalized moderate myasthenia gravis (MGFA-IIa), EMG- D-20%, Ab.AchR- 12 nmol/dl. As thorax CT was equivocal for thymic lymphoid hyperplasia (Fig.3), we requested also a thymic scintigraphy with Tc 99 to appreciate the radiotracer uptake ratio (Fig.4). Heterogenous and moderate absorption also directed the diagnosis to thymus lymphoid hyperplasia. The treatment with 4 tb. of pyridostigmine per day controlled well the myasthenic symptoms. She was operated for GD, undergoing a total thyroidectomy followed by thyroid hormonal substitution. Annual check-up for MG showed that the necessary dose of pyridostigmine decreased to 2 tb. per day.

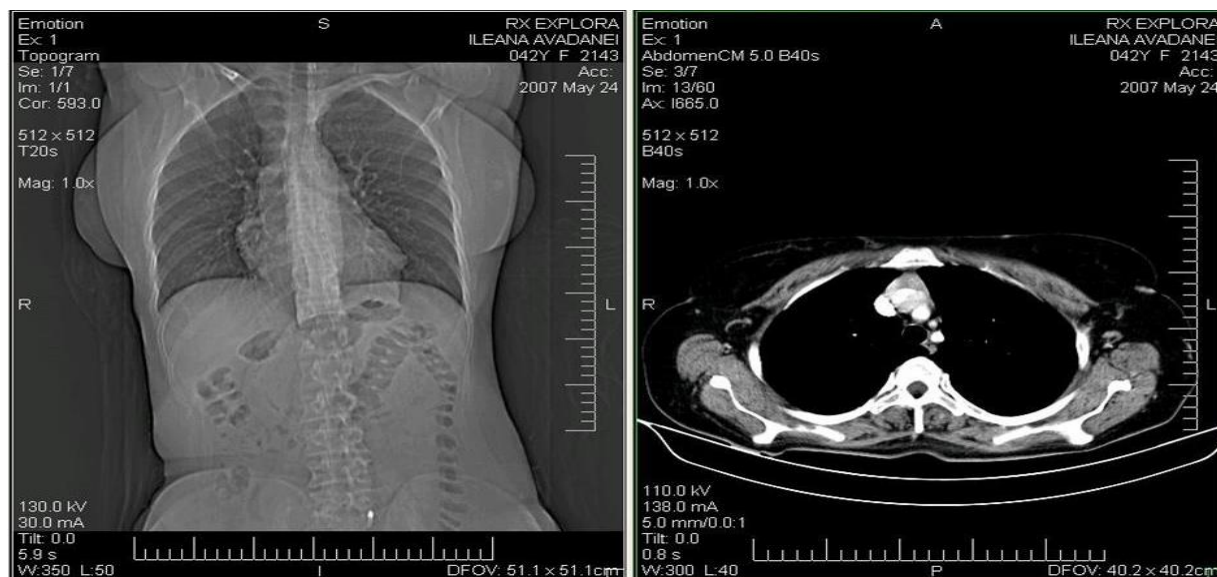


Fig.3 Thorax CT for thymic lymphoid hyperplasia.

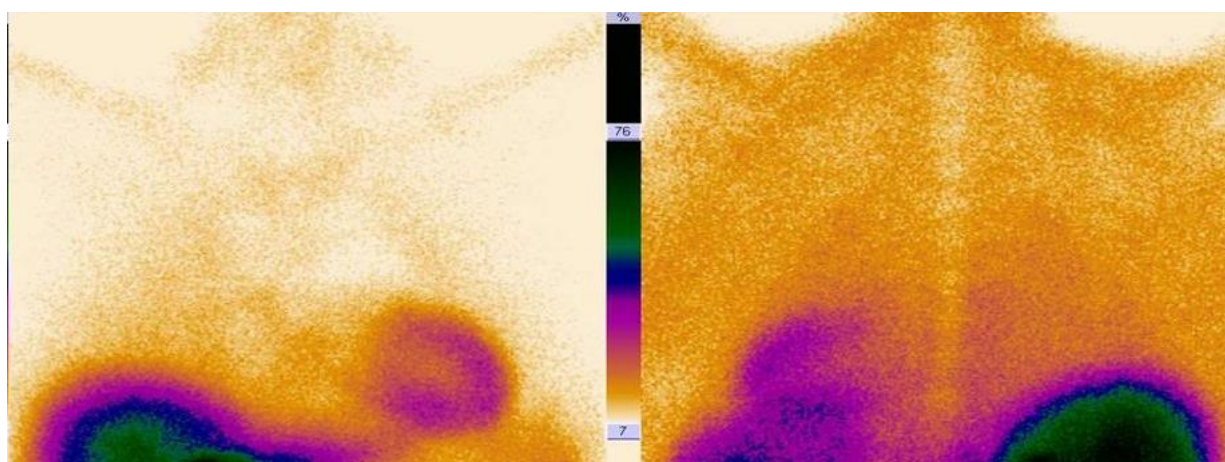


Fig. 4 Thymic scintigraphy- heterogenous absorption



### Case 3

MM, 54-year-old woman having a 9-year-history of GD under medical treatment. After 9 years history of Grave's disease, she was diagnosed with moderate generalized MG (MGFA-IIa). Thyroid profile was TSH-0,1 ui/ml, fT4 - 1,2ng/ml, the cervical CT scan performed revealed diffuse goitre. Myasthenic profile- EMG-D-18%, the thorax CT revealed heterogenous increased size thymic region (Fig.4), Ab.AChR- 8 nmol/dl. antiMuSK-negative.

We performed surgical treatment for GD and in the second stage we perform thymectomy as the repeated CT scan raised the suspicion of thymoma. Extensive thymectomy was performed one year later, pathological report showing benign thymoma (type A- WHO classification). In the postoperative period the myasthenic symptoms were well controlled with 1 tb. of pyridostigmine/day as required.

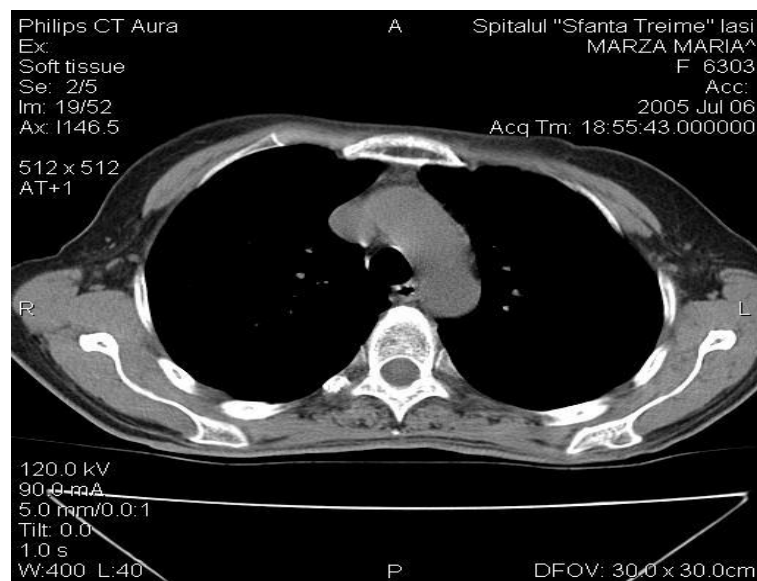


Fig 4. Thorax CT with heterogenous increased size thymic region.

### MG and HT

#### Case 4

UD, 54-year-old woman was admitted for thymectomy after 4 years of progressive worsening MG refractory to medical treatment for 1 month (pyridostigmine 6-8 tb. per day and methylprednisolone 32 mg. every 2 days).

Myasthenic profile- EMG-D-25%, antibody to AChR- 28 nmol/dl, antiMuSK-negative, the thorax CT scan revealed enlarged antero-superior mediastinum with a heterogenous thymic tissue.

HT was diagnosed 1 year back (ab. antiTPO-556UI/ml), compensated with Euthyrox 75ug/day (TSH-2uUI/ml, Ft4- 1,2ng/dl). Thymic scintigraphy showed discrete hyper

fixation of  $^{99m}\text{Tc}$  Tetrofosmin, heterogenous, with vertical trajectory in the left paramedian anterior mediastinum (Fig.5). After 4 sessions of plasmapheresis to improve the myasthenic status an extended thymectomy through longitudinal sternotomy was performed. Pathology report showed atrophic thymus with areas of follicular hyperplasia (Fig 6.). Post-operative course was unfavourable with aggravating respiratory failure necessitating prolonged mechanical ventilation. In Intensive Care Unit any attempt for improving myasthenic symptoms was useless, including nonsteroidal immunosuppression treatment.

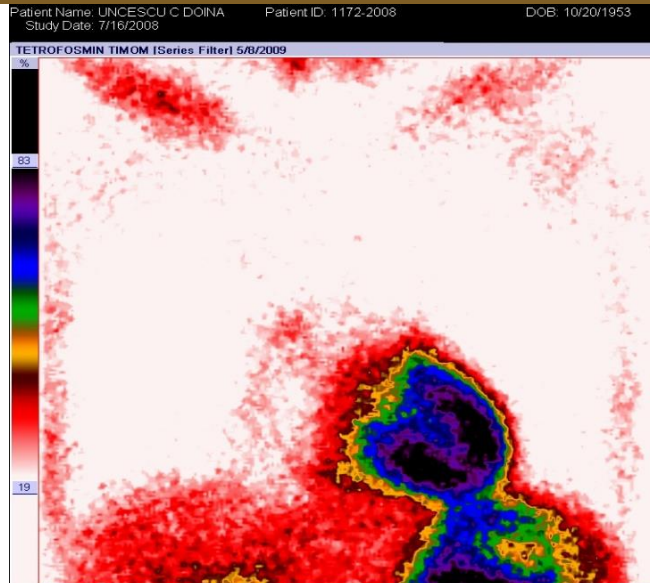


Fig.5 Preoperative thymic scintigraphy

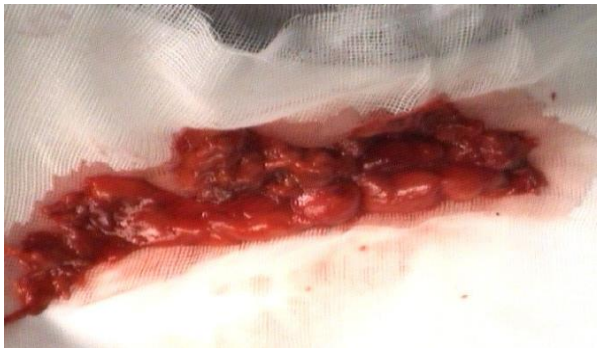


Fig.6 Surgical specimen- nodular aspect of the thymus gland.

Postoperative complications were related with long-term mechanical ventilation and immobilization: ventilator dependent respiratory infection, peri-tracheostomy infection, multiple pressure sores. She died due to multiple organ failure after 2 months of intensive care.

### Case 5

ML, 28-year-old woman, was admitted for thymus surgery, presenting 6 months history of moderate generalized MG and 9 months of HT.

Myasthenic profile-EMG-D-62%, positive anticholinesterase test, Ab .AchR- 6 nmol/dl ( 0,25), CT thorax objectivated nodular thymus (14/11 mm, 14/18 mm) with high index of suspicion for thymoma ( Fig. 7). HT was

well controlled with Euthyrox 50 micrograms/day with AAT-TPO-176,7 (N<50).

She underwent uneventful extended thymectomy, pathology report of the surgical specimen was thymic lymphoid hyperplasia (Fig. 8). At 6 months postoperative check-up she was in complete remission and at annual check-ups the myasthenic status remitted.

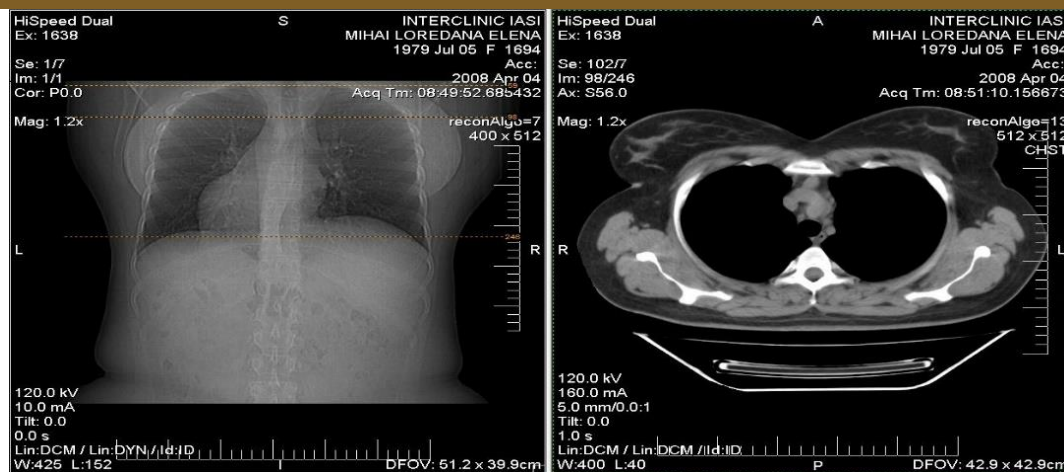


Fig.7 Thorax CT showing enlarged heterogenous thymic gland.

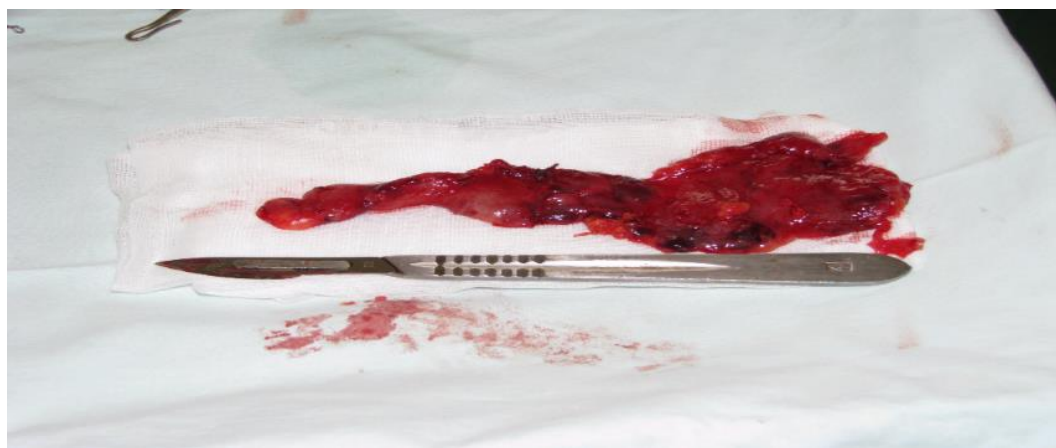


Fig.8 Surgical specimen case 5.

### Case 6

CT, 64-year-old woman presenting a 8 year-history of moderate generalized MG, (MGFA- IIa), Ab.AchR-12nmol/l, well controlled by anticholinesterase drugs was admitted in our clinic following a thorax CT which showed

evident image of invasive thymoma into the left mediastinal pleura ( Fig. 9). HT was well controlled with 100 micrograms of Euthyrox per day.



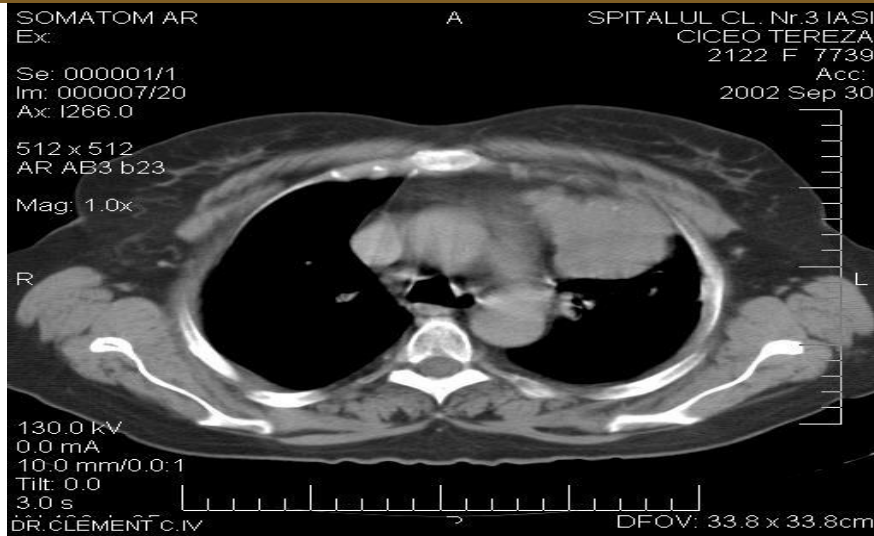


Fig.9 Thorax CT- invasive thymoma

The operation consisted in extensive thymectomy ( Fig.10), with partial excision of the left mediastinal pleura through longitudinal sternotomy. Pathology report revealed B2 invasive thymoma, the limits of excision were microscopically tumour free.

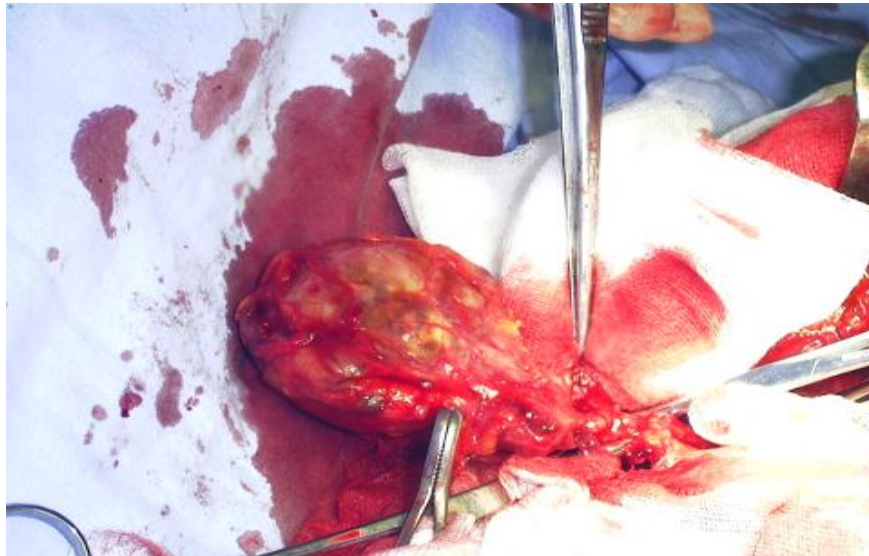


Fig.10 The aspect of the thymic tumour –intra-operative view.

Post-operative course was uneventful, making a good recovery. Postoperative treatment consisted in external radiotherapy, total dose of 44 Gy. followed by 1 year of immunosuppressive treatment as tolerated. After that she presented complete remission of MG for 5 years. In the 6<sup>th</sup> year post-operative MG recurs as mild generalized clinical form, being controlled with 2 tb. of pyridostigmine per day. To rule out a tumour recurrence, a

CT scan was requested no tumour recurrence seen, just fibrous scar tissue retrosternal and inflammatory pericarditis postradiotherapy Fig.11). Thymic scintigraphy showed the lack of radiotracer fixation in the anterior mediastinum, which confirmed the absence of tumour recurrence (Fig.12)



Fig.11 Thorax CT scan

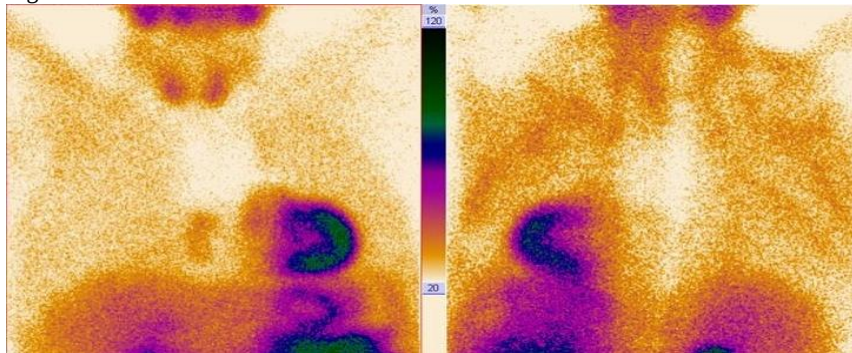


Fig.12 Mediastinal scintigraphy

Due to inflammatory pericarditis she was referred to the cardiologist who kept her under observation for heart failure but in time this aggravated, and she was referred to cardiac surgery for planned pericardiectomy. She died 7 days after cardiac surgery because of cardiorespiratory failure.

## MG-HT-haemolytic anaemia

### Case 7

GE-19-year-old man was under multidisciplinary observation (haematologist and endocrinologist) and treated for autoimmune haemolytic anaemia, HT, MG (MGFA I), Ab.AChR/Ab.Musk seronegative. While HT and

ocular MG were well controlled with medical treatment, haemolytic anaemia with frequent acute exacerbations was a difficult and severe problem as repeated blood transfusions and steroids had only temporary effect.

A cervico-thoracic CT was performed and revealed a mediastinal mass suggestive for thymoma (Fig.13). For that reason, the mediastinal mass was removed through a longitudinal sternotomy. Pathology report showed thymic lymphoid hyperplasia. After thymectomy the haemolytic anaemia remitted.



Fig. 14 CT of the neck – non-compressive goitre, thorax CT- antero-superior mediastinal mass

## MG with toxic multinodular goitre.

### Case 8

AM, 46-year-old woman was diagnosed with moderate generalized MG and toxic multinodular compressive goitre

(Fig.15). Thyroid profile: TSH-0,1 UI/ml, ft4- 1 ng/dl. Thyroid total volume of 65,9 ml. Myasthenic profile- MGFA-IVA, EMG-D-20%, Ab.AChR- 62nmol/dl.



Fig.15 Cervical CT- compressive multinodular goitre. Thorax CT -goitre prolonged retrosternal.



Fig.16 Thorax CT -normal thymic region.

Following a multidisciplinary team meeting, the therapeutic decision was to operate the goitre and to keep patient on anticholinesterase drugs. A total thyroidectomy was done

with good results but in a period of 3 months postoperatively, MG aggravated despite our expectations of improvement after total thyroidectomy.

As we were caught in a difficult situation, we decided for a thymic scintigraphy to see the level of absorption of the radiotracer in the thymic tissue found normal at thorax CT scan (Fig.16). Thymic scintigraphy showing hyper fixation

of Tc in antero-inferior mediastinum (Fig.17). At this stage the diagnosis of ectopic thymoma associated with MG was obvious.

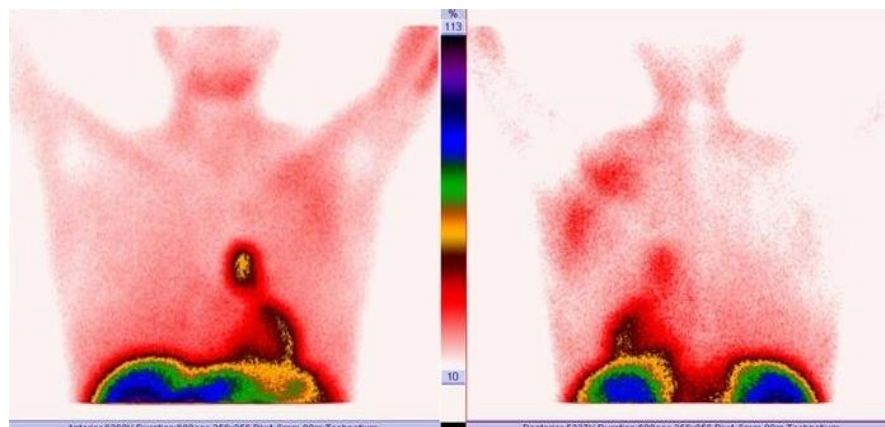


Fig. 17 Thymic scintigraphy

Control thorax CT scan showed an antero-inferior mediastinal mass, which overlapped the location of scintigraph image. Extended thymectomy was performed 6 months after total thyroidectomy with evident improvement of the myasthenic symptoms postoperatively. Pathology report of the surgical specimen (mixt thymoma or AB type - WHO classification, with capsular microscopic invasion). She was referred to the oncologist for further chemotherapy. She refused the treatment and unfortunately, she died 1 year following the thymectomy due to fulminant myasthenic crisis.

## Discussions

MG and GD or HT are autoimmune diseases encountered in clinical practice are quite rare but challenging as therapeutic decision.

In 1908 was published the first study that sustained the association of MG and GD [3]. Since then numerous studies have been recorded regarding the association of autoimmune thyroid diseases with MG, with different result. Yu-Pei Lin et al. [11] using data from the Taiwan's National Health Insurance collected 7695 cases of MG and 52068 cases of Thyroid disorders that concluded MG is associated with all thyroid disorders. The study observed a higher rate of autoimmune thyroid disease in females and a higher strength in older males. In our study we observed the same pattern regarding the sex ratio.

In this series all patients except one, were diagnosed with thyroid disease before the onset of myasthenia gravis.

Murakami M. et al. demonstrated the presence of thymic hyperplasia in GD patients, calculating on CT scan images,

the size and density of the thymus on untreated and treated GD patients. The conclusion was thymic hyperplasia regresses in patients treated either with anti-thyroid drugs or by total thyroidectomy.[12]

Nakamura T. et al. demonstrated by mediastinal biopsy, the presence of thyrotropin receptors in the hyperplastic thymus of a young patient with hyperthyroidism. The presence of these receptors raises the hypothesis that the thymus is also a target organ for the autoimmune aggression in GD. [13]

Thymic hyperplasia is a common and reversible feature in patients with GD and hyperthyroidism. Recognition of the benign nature of TH and its regression following treatment of the hyperthyroidism is important to prevent unnecessary surgical procedures. [14,15,16]

For a better distinction between a thymic lymphoid hyperplasia and thymoma as an anterior mediastinal mass as is usually described to a thorax CT scan, we use thymic scintigraphy, a functional investigation, complementary to CT scan morphological examination. Hyperabsorption of radiotracer is suggestive for thymoma. [17]

Muscle weakness may be present in thyrotoxicosis as well as in MG, so being aware of the possibility of this association will prevent the diagnostic delay and proper treatment.



<sup>99m</sup>Tc MIBI scan is useful in diagnosis and therapeutic strategy of thymic lesions either when conventional imaging investigations fail to confirm a clinical diagnosis or in order to make evidence of the malignancy of the thymic lesion. Based on hypothesis that understanding the radiotracer uptake can correlate with the cellular characteristics of the thymic disorder, scintigraphy can be useful in elucidating the lesion type, with subsequent improvement on therapeutic decision and patient prognosis. [18]

When radiotracer uptake ratio is above 1,5 in the thymic region the diagnosis is likely to be a thymoma. In the case nr. 8, radiotracer uptake ratio was of 3,24, drawing attention to an ectopic thymoma. Considering this index along with clinical severity of MG the therapeutic decision was surgery.

We also use thymic scintigraphy complementary to thorax CT in postoperative period of thymoma patients when myasthenic symptoms recur, to rule out a tumour recurrence. Low uptake index (UR<1) excluded these possibilities, myasthenic symptoms being attributable to extrathymic autoimmunity process (case 6).

## Conclusions

Autoimmune thyroid disease may be associated with thymic hyperplasia, in which no surgical action should be taken, regarding the thymus with thymoma surgical treatment is essential.

When GD and thymoma are associated, total thyroidectomy is advisable instead of medical treatment in which is included beta blockers contraindicated in myasthenia gravis.

Total thyroidectomy and thymectomy can be performed at the same stage if the clinical condition of the patient is fit for both operations and in stages.

The deaths in this series seem to be related with the severity of MG progressing to refractory myasthenic crisis with acute respiratory failure.

The thymic <sup>99m</sup>Tc tetrofosmin scintigraphy can be efficient in diagnosing the thymic lesions when conventional imaging investigations fail to confirm a clinical suspicion. Low uptake below 1,5 is suggestive for thymic lymphoid hyperplasia and above 1,5 is suggestive neoplastic lesions.

## Conflict of Interest

Authors have no conflict of interest to disclose

## Ethical issues

The study was approved by the Ethics Commission of the University Hospital "St. Spiridon" Iasi

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